REMARKS

Substance of Telephone Interview

A telephone interview was conducted on August 3, 2010 between the undersigned attorney and Examiner Popa. The rejection under 35 U.S.C. §103(a) based on Glimcher et al. (US 2002/0059652) ("Glimcher") as the primary reference was discussed.

The undersigned attorney submitted that those skilled in the art would not have been motivated to rely on the teachings of Glimcher directed to XBP-1, and substitute XBP-1 with Blimp, because those skilled in the art would not have considered Blimp and XBP-1 as equivalent markers. Furthermore, because neither the expression of XBP-1 nor Blimp-1 was limited to a particular cell-type, those skilled in the art would not have been motivated to make a Blimp transgenic animal in order to specifically identify and isolate all ASCs, or at least very least, would not have reasonably expected the successful results achieved by the invention.

The Examiner indicated that the rejection could be overcome by a showing of unexpected results, for example, a showing in support of the notion that ASCs cannot be identified when a XBP-1 based reporter is used.

Applicants wish to thank the Examiner for the courtesy and helpful discussion with the undersigned attorney during the telephone interview.

Unobviousness

Applicants respectfully submit that those skilled in the art would not have been motivated to make a XBP-1 transgenic animal in order to specifically identify and isolate ASCs; and even if one were to attempt, an XBP-1 based reporter system would not work to uniquely identify ASCs, because, *inter alia*, XBP-1 is ubiquitously expressed.

Applicants first direct the Examiner to the Nutt Declaration submitted with Applicant's Response dated September 29, 2009. In paragraph 4a of the Declaration, Dr. Nutt stated:

> "While it is my experience that XBP-1 is highly expressed in plasma cells, it was well known in the art prior to the filing of the '321 application that that XBP-1 is highly expressed in a number of other cell types and is highly induced by the cellular stress response system. See, for example, Glimcher, paragraph [0003] states: "*this transcription factor is expressed ubiquitously in adults but is mainly found in exocrine glands and bone precursors in the embryonic mouse...*".

Further, Reimold et al. (*Nature, 412*(6844) :300-307, 2001), previously submitted as Exhibit 3 attached to the Nutt Declaration, also describes XBP-1 as "found ubiquitously in adult tissues, but preferentially expressed in fetal exocrine glands, osteoblasts, chondroblasts and liver." See page 300, column 2, paragraph 2 of Reimold et al. (attached again herewith as courtesy).

Moreover, a review paper from the Glimcher group, Iwakoshi et al. (*Immunol. Rev.* 194: 29-38, 2003, attached hereto), also confirms the ubiquitous expression pattern of XBP-1:

> "X-box binding protein-1 expression
> During murine embryogenesis, in situ hybridization studies revealed a restricted expression of XBP-1 mRNA limited to the skeletal system, exocrine glands such as the pancreas, submandibular, and salivary glands, the liver, whisker follicles, and brown fat (14). XBP-1 is expressed ubiquitously in adult mice with the highest levels of expression found in the lung, liver, spleen, and testis. In a few select organ systems, the levels of transcripts encoding XBP-1 in the adult do vary during development. in developing bone, the varying levels of XBP-1 correlate with that of alkaline phosphatase and tissue inhibitor of metalloproteinase expression, suggesting a potential role for this factor in osteoblast differentiation."
> Page 30, column 2.

Therefore, the evidence in the art at the time overwhelming supports that XBP-1 is ubiquitously expressed, making XBP-1 practically useless as a plasma cell-specific reporter. Clearly, those skilled in the art would not have been motivated to even attempt to use XBP-1 as a

marker in order to specifically identify and isolate ASCs. Further, those skilled in the art would conclude that even if one were to attempt, an XBP-1 based reporter system would not work to uniquely identify ASCs because of the ubiquitous expression pattern of XBP-1.

Applicants also note that in a more recent reference from the Glimcher group, Iwakoshi et al. (*JEM* 204: 2267-2275, 2007, attached hereto) reported high XBP-1 expression in dendritic cells (DCs). These DCs are abundant in the spleen which is also a source for ASCs. Thus, one would expect to "see" a mixture of at least ASCs and DCs, in addition to other cells types in light of the ubiquitous expression pattern of XBP-1.

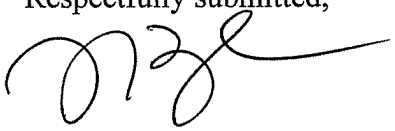
Therefore, the results achieved by the present invention, i.e., identification of ASCs, a rare cell population, are totally unexpected. Applicants have demonstrated that in a Blimp1-GFP transgenic mouse, there was a population of cells which exhibited fluorescence to a uniquely high level in the spleen and in the bone marrow, nearly all of which were ASCs. Further, nearly all ASCs were shown to exhibit fluorescence. Thus, using this unique, high level expression of Blimp-controlled reporter approach, all the ASCs were easily identified.

Not only was the identification of ASCs was unexpected, the extent of enrichment of ASCs was also unexpected. As shown in Example 3 (page 65), the isolation of Blimp^{GFP} expressing ASC gives an enrichment of 100,000 fold over unsorted cells, and provides a virtually definitive method to isolate these rare cells.

Therefore, Applicants respectfully submit that the claimed invention is not obvious in view of the combination of Glimcher, Shaffer, Pol and Mountford. Withdrawal of the rejection under 35 U.S.C. §103(a) is therefore respectfully requested.

Because the instant Supplemental Response complies with 37 C.F.R. §1.111(a)(2), entry thereof is respectfully requested. It is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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